

REMARKS

Upon entry of this response, claims 1-28 are pending in the application. Claim 1 is an independent claim drawn to a micro or nano-particulate drug composition, with claims 2-17 depending therefrom, while claim 18 is an independent claims drawn to a method of making a mirco or nano-particulate drug. The remaining claims (claims 19-28) depend from claim 18.

Claims 1-28 stand rejected as obvious over U.S. Patent No. 6,197,349 to Westesen et al. (the '349 patent).

Applicant respectfully traverses this rejection and respectfully request reconsideration and withdrawal thereof.

Rejection of Claims 1-28 Under 35 U.S.C. 103(a)

Claims 1-28 stand rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 6,197,349 to Westesen et al. (the '349 patent) for the reasons set forth in the Office Action.

RESPONSE

Applicant respectfully traverses this rejection and requests reconsideration and withdrawal thereof.

The reference of record, Haslwanter et al., does not teach or suggest Applicants' inventive subject matter as a whole, as recited

in the claims. Further, there is no teaching or suggestion in this reference which would lead the ordinary skilled artisan to modify the reference to derive the subject matter as defined in the amended claims.

The U.S. Supreme Court in *Graham v. John Deere Co.*, 148 U.S.P.Q. 459 (1966) held that non-obviousness was determined under § 103 by (1) determining the scope and content of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the art; and, (4) inquiring as to any objective evidence of nonobviousness.

To establish a *prima facie* case of obviousness, the Examiner must establish: (1) that some suggestion or motivation to modify the references exists; (2) a reasonable expectation of success; and (3) that the prior art references teach or suggest all the claim limitations. Amgen, Inc. v. Chugai Pharm. Co., 18 USPQ2d 1016, 1023 (Fed. Cir. 1991); In re Fine, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988); In re Wilson, 165 USPQ 494, 496 (C.C.P.A. 1970).

A *prima facie* case of obviousness must also include a showing of the reasons why it would be obvious to modify the references to produce the present invention. See Ex parte Clapp, 277 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). The Examiner bears the initial

burden to provide some convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings. Id. at 974.

A. The Present Inventive Subject Matter

Independent claim 1 is drawn to a micro- or nano-particulate drug composition comprising: a drug substance and a surfactant. The surfactant and the drug substance **form a surfactant-drug substance matrix** at a temperature above the matrix's melting temperature and the surfactant is miscible with the drug substance and does not chemically bond with the drug substance. In addition, the drug substance and the surfactant form a non-crystalline substance or micro- or nano-sized crystals containing the drug substance **while being cooled to room temperature under a shearing force**. Likewise, independent claim 18 is drawn to a method of making a micro and nano-particulate drug comprising the steps of: providing a drug substance-surfactant mixture; melting the mixture at a temperature above the mixture's melting temperature; and cooling the mixture under high shear to approximately room temperature, wherein a non-crystalline substance forms or crystals precipitate coated with said surfactant during crystallization. The remaining claims depend from either claim 1 or 18, and

therefore contain all of the limitations found therein.

B. The Prior Art

Westesen et al. (U.S. Patent No. 6,197,349) disclose particles comprising a supercooled melt of a poorly water-soluble substance and a stabilizing agent. The particles have a mean particle size of between 30 and 500 nm and disperse compositions containing them as delivery vehicles.

C. Differences Between Claimed Inventive Subject Matter and Cited Prior Art

Based on their distinct disclosures and the presently claimed subject matter, Applicant respectfully submits that the '349 patent fails to render obvious the claims, as the '349 patent fails to teach every limitation found in the claims and offers no motivation or teaching to modify the reference in an attempt to achieve the claimed subject matter.

As is seen in claim 1, it is an important aspect of the present inventive subject matter that the novel micro- or nano-particulate drug compositions include **a surfactant-drug substance matrix** as discussed above. Further, the drug substance and the surfactant matrix is formed **while being cooled to room temperature**

under a shearing force. The formation of the surfactant-drug substance matrix by this method aids in the solubility of the drugs. As support for the importance of cooling the mixture under shear force, the present application states that "cooling **under high shear must occur until the eutectic mixture is cooled to a temperature at or around room temperature.** Using this process, micro- and nano-particulate drug crystals will form coated with surfactant during the crystallization process. **If cooling does not occur under high shear until the mixture is cooled to at or around room temperature, crystals will grow on the exterior of the surfactant. Surfactant with crystals on the exterior have very poor dissolution.**" (page 21, lines 2-11). Emphasis added. Thus, the inventive aspects of the present claims require **cooling under high shear** in order to obtain a product with proper dissolution properties. Applicant respectfully submits that the '349 patent does not disclose these limitations, and there would be no motivation for a skilled artisan looking at the patent to do so.

The Examiner argues that the '349 patent discloses the limitations of the claimed subject matter. In particular, the Examiner indicates that the patent teaches "preparing a dispersion of water-insoluble drug with a stabilizer (such as surfactants), which is then emulsified above the melting point of the substance

or mixture of substances (col. 10, lines 1-26) and then subject to vortexing (which reads on shear force) resulting in fine particle preparation." (Page 2 of the office action). However, a careful reading of the '349 patent fails to reveal **any discussion regarding cooling a mixture under high shear force.** The citations made by the Examiner discuss the vortexing of the mixture for emulsification and/or predispersion, but there is **no discussion regarding cooling the mixture under high shear force.** Thus, Applicant respectfully submits that the product obtained by the method in the patent **will not be the same as the claimed product,** since the methods are different. As such, Applicant submits that the Examiner has failed to show that the reference teaches each of the claimed limitations.

In addition, Applicant respectfully submits that one of ordinary skill in the art would not be lead by the patent to attempt cooling the mixture under high shear. As is stated above, the vortexing of the mixture in the patent is done **to achieve emulsification of the mixture,** and therefore is done at high temperatures. No mention is made in the patent regarding the need to continue applying a high shear rate **as the mixture is cooled,** since the emulsification takes place at a higher temperature. Therefore, there is no motivation for a skilled artisan to continue

applying the high shear rate as the mixture is cooled.

Further, Applicant submits that the '349 patent teaches items that are not concerned with the present claims, namely the patent is concerned with wettability and emulsions, which are outside the scope of the present claims. Thus, the patent is concerned with items not addressed by the present claims, and one of ordinary skill in the art again would not be motivated to modify the patent in an attempt to achieve the presently claimed subject matter.

Therefore, Applicants respectfully submit that the '349 patent fails to teach each and every claimed limitation in the independent claims (and also the dependent claims), and that there is no motivation within the patent to modify it in an attempt to achieve the presently claimed subject matter. Thus, the Examiner has failed to meet the burden of proving a *prima facie* case of obviousness.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims as being obvious over the '349 patent.

CONCLUSION

In view of the foregoing, applicants respectfully request the Examiner to reconsider and withdraw the all pending rejections, and

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to allow all of the claims pending in this application.

If the Examiner has any questions or comments regarding this matter, he is welcomed to contact the undersigned attorney at the below-listed number and address.

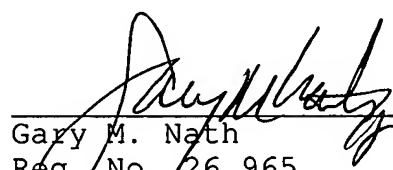
Respectfully submitted,
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